Citation:

Brion MJ, Ness AR, Davey Smith G, Emmett P, Rogers I, Whincup P, Lawlor DA. Sodium intake in infancy and blood pressure at seven years: Findings from the Avon Longitudinal Study of Parents and Children. *Eur J Clin Nutr.* 2008 Oct; 62 (10): 1,162-1,169.

PubMed ID: 17622260

Study Design:

Prospective cohort study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To prospectively assess associations between sodium intake in infancy and blood pressure at seven years in the Avon Longitudinal Study of Parents and Children (ALSPAC).

Inclusion Criteria:

- At seven years of age, all children enrolled with ALSPAC, including those in CIF, were invited to the clinic for examination
- Final analyses on children with complete information on all confounders totaled 533 children at four months and 710 children at eight months.

Exclusion Criteria:

None specifically mentioned. Authors note that a full description of the methodology is published elsewhere.

Description of Study Protocol:

Recruitment

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a contemporary cohort that affords the possibility of investigating early dietary measures and later health in children, and has the overall aim of investigating the health and development of children. This study used a sub-sample of children enrolled in ALSPAC on whom detailed nutritional intake in infancy and early childhood was prospectively collected.

- Pregnant women residing in three health districts located around the city of Bristol with an expected date of delivery between April 1, 1991 and December 31, 1992 were invited to take part in the study

- Of 13,678 singleton, live born children, 1964 who were born in the last six months of the recruitment period were chosen at random to be invited to join the Children in Focus (CIF) study on whom detailed dietary information and growth patterns was collected repeatedly during infancy and early childhood
- Data are available in 1,394 singleton children from at least one CIF clinic
- At seven years of age, all children enrolled with ALSPAC, including those in CIF, were invited to the clinic for examination
- Final analyses on children with complete information on all confounders totaled 533 children at four months and 710 children at eight months.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Information on all foods and drink were recorded in household measures and obtained from CIF infants at four and eight months of age
- Three-day food diaries were used for dietary assessment at eight months and one-day diaries were used at four months, completed by the main caregiver
- Mothers of breastfed infants were asked to record each feed and feed duration
- Sodium intakes were calculated based on manufacturer information, McCance & Widdowson's food tables using microdiet nutritional analysis software
- Dietary supplements were not included in this analysis, only a minority of infants in CIF were receiving supplements by eight months.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Correlation coefficients were calculated for sodium, potassium and energy at four and eight months
- Linearity of relationship between sodium, blood pressure and confounders was assessed from means or prevalence of confounders per quarter of sodium intake and blood pressure
- Means are presented for continuous confounders that have been collapsed into binary variables
- Multiple linear regression was used to investigate the relationship between sodium intake and blood pressure, with cumulative adjustments for confounders
- Primary analysis focused on energy-adjusted sodium intake (adjusting for energy in all models) with secondary analyses using the sodium/potassium ratio and absolute sodium intake.

Data Collection Summary:

Timing of Measurements

- Sodium intake measured at four and eight months of age

- Blood pressure measured at seven years of age.

Dependent Variables

Blood pressure measured using Dinamap 9301 Vital Signs Monitor.

Independent Variables

- Information on all foods and drink were recorded in household measures and obtained from CIF infants at four and eight months of age
- Three-day food diaries were used for dietary assessment at eight months and one-day diaries were used at four months, completed by the main caregiver
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Control Variables

- Birth weight and sex
- Gestational age and child age
- Maternal smoking
- Familial socioeconomic position (maternal age at birth, family social class, maternal and paternal education, parity)
- Potassium intake
- Breastfeeding
- Energy intake.

Description of Actual Data Sample:

- *Initial N:* 745 children total were included in the analysis, 533 children with sodium data at four months and 710 children with sodium at eight months
- *Attrition (final N):* As above
- *Age:* Children measured at seven years of age
- *Ethnicity:* Not mentioned
- *Other relevant demographics: N/A*
- *Anthropometrics:*
    - Mothers of children not included in the analysis were more likely to be younger and to have smoked during pregnancy and were less likely to have breastfed their child, to have a degree and to have a partner with a degree
    - Children not included in the analysis were also more likely to have come from a family of manual social class
    - No differences between those included and excluded for analysis were observed for blood pressure, birth weight, gestational age, sex or maternal parity.
- *Location:* Southwest England.

Summary of Results:

Multivariable Associations of Energy-adjusted Sodium Intake in Infancy with Blood

Pressure at Seven Years

Variables	Systolic Blood Pressure	Diastolic Blood Pressure
Sodium Intake at four months-Model 1	β=0.54, P=0.02	β=0.25, P=0.1
Sodium Intake at four months-Model 2	β=0.55, P=0.02	β=0.26, P=0.1
Sodium Intake at four months-Model 3	β=0.56, P=0.02	β=0.27, P=0.1
Sodium Intake at four months-Model 4	β=0.46, P=0.07	β=0.19, P=0.3
Sodium Intake at four months-Model 5	β=0.45, P=0.08	β=0.18, P=0.3
Sodium Intake at four months-Model 6	β=0.61, P=0.03	β=0.24, P=0.2
Sodium Intake at eight months-Model 1	β=-0.05, P=0.1	β=0.02, P=0.3
Sodium Intake at eight months-Model 2	β=-0.05, P=0.2	β=0.02, P=0.5
Sodium Intake at eight months-Model 3	β=-0.05, P=0.2	β=0.02, P=0.5
Sodium Intake at eight months-Model 4	β=-0.05, P=0.2	β=0.02, P=0.5
Sodium Intake at eight months-Model 5	β=-0.04, P=0.2	β=0.02, P=0.5
Sodium Intake at eight months-Model 6	β=-0.01, P=0.7	β=0.04, P=0.1

Model 1: Adjusted for energy intake at four or eight months, age at blood pressure measurement and sex

Model 2: Model 1 plus socioeconomic position (maternal and paternal education, family social class, maternal age at child birth, parity)

Model 3: Model 2 plus birth weight, gestational age

Model 4: Model 3 plus breastfeeding

Model 5: Model 4 plus smoking during pregnancy

Model 6: Model 5 plus sodium intake at seven years.

Other Findings

- Sodium intake at four months ranged from 3.1 to 19.2mmol per day with a mean of 7.2mmol

per day
- Sodium intake at eight months ranged from 3.5 to 116.6mmol per day with a mean of 23.1mmol per day
- 0.4% of participants at four months and 73.0% at eight months exceeded recommended levels for infant sodium intake
- At four months, 257 (48.2%) infants were being breastfed and 467 (87.6%) had mixed feeding
- At eight months, 186 (26.2%) infants were being breastfed, with all infants having mixed feeding
- Mean systolic blood pressure at seven years in children assessed at four or eight months was 98.4±9.4mmHg and mean diastolic blood pressure was 56.4±6.7mmHg
- After minimal adjustment, sodium intake at four months was positively associated with systolic blood pressure at seven years (ß=0.54mmHg/mmol,95% CI: 0.09, 0.98mmHg, P=0.02)
- This changed little following adjustment for confounders but attenuated after adjusting for breastfeeding
- This association was not mediated by sodium intake at seven years
- Due to high sodium-potassium correlations, effects of sodium independent of potassium could not be estimated with reasonable precision
- Sodium intake neither at eight months nor seven years was associated with systolic blood pressure at seven years.

Author Conclusion:

- In conclusion, we have found that at eight months of age, a large proportion of participants in this cohort of children born in the early 1990s were exceeding the maximum recommended intake for sodium in infancy
- We found some evidence that greater sodium intake in infancy is associated with elevated blood pressure in later life; however, this was found for sodium intake at four months only despite almost all infants at this age consuming below the maximum recommended intake
- Further studies are required to confirm this finding before one could conclude that infancy is a sensitive period with respect to the effect of dietary sodium intake on later blood pressure.

Reviewer Comments:

Authors note that the association between sodium intake at four months and later systolic blood pressure may be a chance finding. Before the age of four months, infants are less efficient at excreting excess sodium and healthy infants only begin to excrete an excessive sodium load at around four months. Authors also note the following:

- *Gold standard for measurement of sodium is 24-hour urinary sodium, which is difficult to implement in infants and not feasible in population studies*
- *Assessment of breast milk sodium assumes similar concentrations for all women and any measurement error in breast milk assessment would affect the four-month intake more than the eight-month intake due to the higher proportion of sodium attributable to breast milk at four months.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	???
2.2.	Were criteria applied equally to all study groups?	N/A
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	N/A
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	???
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	???
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes